AF/1615

CASE 47-19658/A

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

29/Appeal Brief (4)
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IN RE APPLICATION OF

BRUGGER ET AL.

Art Unit: 1615

Examiner: R. Bawa

APPLICATION NO: 08/288,415

FILED: AUGUST 9, 1994

FOR: AN AEROSOL CONTAINER AND A METHOD FOR STORAGE AND ADMINISTRATION OF A PRE-DETERMINED AMOUNT OF A PHARMACEUTICALLY ACTIVE AEROSOL

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4-25-00

Assistant Commissioner for Patents
Washington, D.C. 20231

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APPELLANTS' APPEAL BRIEF

Pursuant to 37 C.F.R. 1.192, and pursuant to the Notice of Appeal filed January 28, 2000, this paper constitutes Appellants' Brief on Appeal before the Board of Patent Appeals and Interferences. The appealed claims are set forth in the attached Appendix. Appellants submit this Appeal Brief in triplicate, along with the requisite fee of $310.00. Favorable consideration of this appeal is earnestly solicited.

I. Real Party in Interest

The real party in interest for the appealed application is Novartis AG, a corporation organized under the laws of Switzerland.

II. Related Appeals and Interferences

Appellants are aware of no other appeals or interferences that will directly affect or be directly affected by or have a bearing on the Board's decision in this pending appeal.

III. Status of Claims

The status of the claims in this application is as follows:

A. Claims pending on appeal - Claims 2-15.

B. Claims canceled - Claim 1.

IV. Status of Amendments

No amendments were presented to the Examiner after the Final Rejection in the present application..

V. Summary of Invention

Appellants' invention relates to an aerosol container for the storage and administration of pharmaceutically active aerosols. Over the past years, it has been considered desirable to phase out the use of fluorochlorohydrocarbons as propellant gases in aerosol containers, including aerosol containers for medicinal compositions. Although alternative propellant gases are now in use, with those alternative propellant gases, pharmaceutically active agents tend to adhere to and build-up on the inner container wall. This presents a problem for proper administration of the pharmaceutically active agent, in that such deposits on the inner container wall may result in the desired amount of pharmaceutically active agent not being present in the metering chamber for delivery. A further consequence is that the total amount of pharmaceutically active agent stored in the container cannot be administered, since a very considerable proportion of the total amount of the pharmaceutically active agent may remain deposited on the inner wall of the container. Appellants' invention addresses such problems by applying to the "inner" wall of the container a plastics coating which inhibits the pharmaceutically active agent from depositing thereon.

As defined in claim 15, Appellants' invention therefore relates to an aerosol container system for metering and administering pharmaceutically active aerosols supplied in the form of a suspension. The suspension includes a pharmaceutically active agent and a propellant gas free of fluorochlorohydrocarbons (specification, page 2, lines 12-16 and 21-24), said aerosol container system comprising a container for storing the suspension comprising a container wall, the inner portion of said container wall which defines the interior of the container being coated with a plastics coating which inhibits the pharmaceutically active agent in the suspension from depositing thereon (specification, page 2, lines 21-27); and a metering valve system for dosing and releasing the suspension comprising a metering chamber and a valve stem, said valve stem capable of being displaced from a first position to a second position, wherein in the first position the valve stem affords communication between the interior of the container and the metering chamber while

simultaneous blocking communication between the metering chamber and the outside of the aerosol container system such that the metering chamber can be filled with a dose of the suspension from the container (specification, page 3 line 29 to page 4, line 6), and wherein in the second position the valve stem blocks communication between the interior of the container and the metering chamber while simultaneously affording communication between the metering chamber and the outside of the aerosol container system such that the dose of suspension in the metering chamber can be released from the aerosol container system (specification, page 4, lines 10-26).

Claim 2 is dependent on claim 15 and recites that the plastics coating is polytetrafluoroethylene or perfluoroethylenepropylene (specification, page 2, lines 27-29).

Claim 3 is dependent on claim 15 and recites that the thickness of the container wall is in the range from approximately 0.1 mm to approximately 2 mm, and the thickness of the plastics coating is in the range from approximately 1 nm to approximately 1 mm (specification, page 2, lines 31-33).

Claim 4 is dependent on claim 15 and recites that the volume of the interior of the container is in the range from approximately 1 ml to approximately 100 ml and the volume of the metering chamber is from approximately 5 µl to approximately 400 µl (specification, page 3, lines 6-8).

Claim 5 is dependent on claim 15 and recites a method for the storage and administration of a pharmaceutically active aerosol in the form of a suspension, wherein the suspension includes a pharmaceutically active agent and a propellant gas that is free of fluorochlorohydrocarbons (specification, page 2, lines 21-23).

Claim 6 is dependent on claim 5 and recites that the pharmaceutically active agent in the suspension is an anti-asthmatically active agent (specification, page 6, lines 1-2).

Claim 7 is dependent on claim 6, and recites that the anti-asthmatically active agent is selected from the group consisting of formoterol, formoterol fumarate, and corticosteroids (specification, page 6, lines 9-14).

Claim 8 is dependent on claim 6 and recites that the anti-asthmatically active agent is (1R,2S)-(3E,5Z)-7-[1-3-trifluoromethylphenyl)-1-hydroxy-10-(4-acetyl-3-hydroxy-2-propylphenoxy)-3,5-decadien-2-ylthio]-4-oxo-4H-1-benzopyrane-2-carboxylic acid or the sodium salt thereof (specification, page 6, lines 15-18).

Claim 9 is dependent on claim 15 and recites an aerosol container system wherein the propellant gas consists essentially of fluorohydrocarbons (specification, page 2, lines 22-25).

Claim 10 is dependent on claim 15 and recites that the suspension further includes cosolvents and/or surfactants (specification, page 2, lines 21-25).

Claim 11 is dependent on claim 3 and recites that the thickness of the container system wall is approximately 0.4 mm and the thickness of the plastics coating is approximately 10 nm (specification, page 3, lines 6-8).

Claim 12 is dependent on claim 5 and recites that the propellant gas consists essentially of fluorohydrocarbons (specification, page 2, lines 22-25).

Claim 13 is dependent on claim 5 and recites that the suspension further includes cosolvents and/or surfactants (specification, page 2, lines 21-25).

Claim 14 is dependent on claim 7 and recites that the anti-asthmatically active agent includes the corticosteroid 9α-chloro-6α-fluoro-11β,17α-dihydroxy-16α-methyl-3-oxo-androsta-1,4-diene-17β-methoxycarbonyl-17-propionate (page 3, lines 8-11).

VI. Issues

A. Whether claims 3-15 are unpatentable under 35 U.S.C. 103 over Gennaro (Pharmaceutical Sciences) in view of Stetz (U.S. Patent No. 2,815,889).

B. Whether dependent claim 2 is unpatentable under 35 U.S.C. 103 over Gennaro (Pharmaceutical Sciences) in view of Stetz (U.S. Patent No. 2,815,889).

VII. Grouping of Claims

For the purposes of this appeal, claims 3-15 stand and fall together. These claims are separately patentable from claim 2.

Claim 2 is separately patentable from claims 3-15. Claim 2 does not stand or fall with claims 3-15.

VIII. Argument

In the Final Rejection, the Examiner rejected claims 2-15 under 35 U.S.C. 103 as being unpatentable over Gennaro in view of Stetz. Appellants respectfully traverse this rejection.

The rejection appears to rely primarily on Gennaro, which is a general reference related to aerosol packaging of pharmaceutical products. According to the Examiner, Gennaro discloses aerosol containers having "protective coatings" and valves analogous to those claimed. The Examiner relies on Stetz for the teaching of a metering device controlling discharge from aerosol cans, and concludes that it would have been obvious to one of ordinary skill in the art to use the metering device of Stetz in the aerosol cans disclosed by Gennaro.

The rejection should be reversed as Gennaro and Stetz fail to teach or suggest Appellants' claimed aerosol container system having a plastics coating located on the interior wall, where the plastics coating "inhibits the pharmaceutically active agent in the suspension from depositing thereon." Instead, Gennaro only states in general terms that a "protective coating" may prevent water and other corrosive materials from attacking tin containers, and that such a coating may make aluminum containers less reactive. See Gennaro, page 1670. Gennaro remains silent regarding the selection of coatings for the container that will inhibit the deposition of a pharmaceutically active agent thereon.

Stetz fails to remedy Gennaro's deficiency as Stetz makes no mention of any coating for the interior of an aerosol can. Accordingly, Stetz also fails to teach or suggest a coating that specifically inhibits the pharmaceutically active agent from depositing on the walls of the container.

It is well settled that, to sustain a rejection under section 103, the prior art must teach or suggest every limitation of an applicant's claims. MPEP 2143.03. Although Gennaro exemplifies oleoresin, phenolic, vinyl, or epoxy coatings, Gennaro offers no indication as to whether such coatings may be used, or are intended to be used, to inhibit deposition of pharmaceutically active agents.

Further, the Examiner's vague and conclusory characterization of Gennaro's coatings as "analogous" to Appellants' claimed plastic coating (see Final Rejection, page 2) does not adequately address Appellants' express recitation regarding inhibiting deposition of the pharmaceutically active agent. The mere fact that Gennaro's coatings, even if accurately considered "analogous," could have been modified to inhibit the deposition of pharmaceutically active agents would not have made modification of Gennaro's coatings obvious unless the prior art would have suggested the desirability of such a modification. *See, e.g., In re Laskowski*, 10 U.S.P.Q.2d 1276, 1278 (Fed. Cir. 1987). Because Gennaro and Stetz do not even mention inhibiting deposition of pharmaceutically active agents, the alleged "analogous" nature of the coatings would have done nothing to motivate the skilled artisan to substitute a coating as recited in Appellants' claim 15 for Gennaro's coatings.

Appellants also disagree that Gennaro's coatings can be considered "analogous" to the claimed plastics coatings. As mentioned, Gennaro's coatings are designed to prevent water and other corrosive materials from attacking or reacting with a container. In contrast, Appellants' plastics coatings are selected to inhibit deposition of pharmaceutically active agent in a container. The prevention of corrosion in Gennaro is not analogous to and does not remotely suggest the desirability of preventing the deposition of pharmaceutically active agents in aerosol containers.

The rejection under section 103 is additionally flawed as it fails to consider Appellants' claimed invention as a whole. As mentioned, Appellants' claimed invention addresses a problem

that occurs when fluorochlorohydrocarbon propellants are replaced with fluorohydrocarbon propellants. With fluorohydrocarbon propellants, pharmaceutically active ingredients tend to adhere to the inner surface of the aerosol container. Appellants' claims therefore recite the use of a plastics coating that inhibits deposition of pharmaceutically active agents thereon, in a system having a propellant gas free of fluorochlorohydrocarbons.

Gennaro and Stetz do not mention any problem related to the use of propellants free of fluorochlorohydrocarbons. Gennaro and Stetz do not mention any connection between deposition of pharmaceutically active agents and the use of propellants free of fluorochlorohydrocarbons. Gennaro and Stetz also do not identify any coating as inhibiting deposition of pharmaceutically active agents within the container. In this regard, Gennaro and Stetz clearly fail to support the bare conclusion that the "cited art is analogous because it . . . is reasonably pertinent to the particular problem with which the inventor is involved." See Final Rejection, page 2.

To the extent the Examiner takes the position that Gennaro's coatings *inherently* prevent the deposition of pharmaceutically active agent, the record does not support such a position. As explained by the Federal Circuit:

> Inherency, however, may not be established by probabilities or possibilities. The mere fact that a certain thing may result from a given set of circumstances is not sufficient. If, however, the disclosure is sufficient to show that the natural result flowing from the operation as taught would result in the performance of the questioned function, it seems to be well settled that the disclosure should be regarded as sufficient.

Continental Can Co. USA v. Monsanto Co., 20 U.S.P.Q.2d 1746, 1749 (Fed. Cir. 1991 (quoting *In re Oelrich*, 212 U.S.P.Q. 323, 326 (C.C.P.A. 1981)) [emphasis added].

Here, Gennaro only discusses the ability of his coatings to prevent water and corrosive ingredients from attacking tin surfaces of a container, and the coatings' ability to lessen reactivity of aluminum surfaces of the container. Gennaro does not state whether his coatings prevent deposition of a pharmaceutically active agent in the container. Without a disclosure in the prior art sufficient to show that prevention of the pharmaceutically active agent's deposition would invariably occur due to Gennaro's coatings, a proper case of inherency has not been presented. At best, an inherency argument based on the cited prior art would amount to an unsupported contention that Gennaro's coatings might inhibit deposition of pharmaceutically active agents in an aerosol container. As stated in *Continental Can*, however, inherency cannot be established by probabilities alone.

Claim 2 specifies that the plastics coating is polytetrafluoroethylene or perfluoroethylenepropylene. Claim 2 is separately patentable from claims 3-15 because prior art

anticipating or rendering obvious claims 3-15 would not necessarily anticipate or render claim 2 obvious.

Gennaro and Stetz additionally fail to teach or suggest the plastics coatings recited in claim 2, i.e., a plastic coating that is polytetrafluoroethylene or perfluoroethylenepropylene. Again, all claim limitations must be taught or suggested to sustain a rejection under section 103. MPEP 2143.03. Further, where the prior art may possibly disclose a genus embracing a claimed species, motivation to select the species does not necessarily exist to support a proper rejection under section 103. *See In re Baird*, 29 U.S.P.Q.2d 1550, 1552 (Fed. Cir. 1994). Conservatively, the oleoresin, vinyl, or epoxy coatings briefly mentioned by Gennaro embrace thousands of polymers. Gennaro and Stetz do not appreciate the problems associated with the replacement of fluorochlorohydrocarbons with alternative gas propellants. Consequently, nothing in either Gennaro or Stetz, alone or in combination, would have motivated the skilled artisan to select polytetrafluoroethylene or perfluoroetheyllenepropylene as coatings for use in an aerosol can. For at least these reasons, claim 2 is clearly patentable over Gennaro and Stetz.

IX. Conclusion

In view of the foregoing, it is respectfully submitted that the Examiner's Final Rejection of claims 2-15 is clearly erroneous and should be reversed. Reversal of the outstanding Final Rejection is earnestly solicited.

Respectfully submitted,

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APPENDIX

2. An aerosol container system according to claim 15, wherein the plastics coating is polytetrafluoroethylene or perfluoroethylenepropylene.

3. An aerosol container system according to claim 15, wherein the thickness of the container wall is in the range from approximately 0.1 mm to approximately 2 mm, and the thickness of the plastics coating is in the range from approximately 1 nm to approximately 1 mm.

4. An aerosol container system according to claim 15, wherein the volume of the interior of the container is in the range from approximately 1 ml to approximately 100 ml and the volume of the metering chamber is from approximately 5 µl to approximately 400 µl.

5. Method for the storage and administration of a pharmaceutically active aerosol in the form of a suspension, the suspension including a pharmaceutically active agent and a propellant gas that is free of fluorochlorohydrocarbons, wherein a container system according to claim 15 is used.

6. Method according to claim 5, wherein the pharmaceutically active agent in the suspension is an anti-asthmatically active agent.

7. Method according to claim 6, wherein the anti-asthmatically active agent is selected from the group consisting of formoterol, formoterol fumarate, and corticosteroids.

8. Method according to claim 6, wherein the anti-asthmatically active agent is (1R,2S)-(3E,5Z)-7-[1-3-trifluoromethylphenyl)-1-hydroxy-10-(4-acetyl-3-hydroxy-2-

propylphenoxy)-3,5-decadien-2-ylthio]-4-oxo-4H-1-benzopyrane-2-carboxylic acid or the sodium salt thereof.

9. An aerosol container system according to claim 15, wherein the propellant gas consists essentially of fluorohydrocarbons.

10. An aerosol container system according to claim 15, wherein the suspension further includes cosolvents and/or surfactants.

11. An aerosol container according to claim 3, wherein the thickness of the container system wall is approximately 0.4 mm and the thickness of the plastics coating is approximately 10 nm.

12. Method according to claim 5, wherein the propellant gas consists essentially of fluorohydrocarbons.

13. Method according to claim 5, wherein the suspension further includes cosolvents and/or surfactants.

14. Method according to claim 7, wherein the anti-asthmatically active agent includes the corticosteroid 9α-chloro-6α-fluoro-11β,17α-dihydroxy-16α-methyl-3-oxo-androsta-1,4-diene-17β-methoxycarbonyl-17-propionate.

15. An aerosol container system for metering and administering pharmaceutically active aerosols supplied in the form of a suspension, the suspension including a pharmaceutically active agent and a propellant gas free of fluorochlorohydrocarbons, said aerosol container system comprising:

a container for storing the suspension comprising a container wall, the inner portion of said container wall which defines the interior of the container being coated with a plastics coating which inhibits the pharmaceutically active agent in the suspension from depositing thereon, and

a metering valve system for dosing and releasing the suspension comprising a metering chamber and a valve stem, said valve stem capable of being displaced from a first position to a second position,

wherein in the first position the valve stem affords communication between the interior of the container and the metering chamber while simultaneous blocking communication between the metering chamber and the outside of the aerosol container system such that the metering chamber can be filled with a dose of the suspension from the container, and

wherein in the second position the valve stem blocks communication between the interior of the container and the metering chamber while simultaneously affording communication between the metering chamber and the outside of the aerosol container system such that the dose of suspension in the metering chamber can be released from the aerosol container system.